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SERIAL NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.
08/869,406	06/05/97	BARNIKOL W	DT-2179

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HM11/0605

EXAMINER
GUPTA, A

ART UNIT	PAPER NUMBER
1654	19

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

DATE MAILED: 06/05/98

☐ This application has been examined ☐ Responsive to communication filed on 03-30-98 ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 MONTHS from the date of this letter.
Failure to respond within the time period will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENTS ARE PART OF THIS ACTION:

1. ☐ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice re Patent Drawing, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449
4. ☐ Notice of Informal Patent Application, Form PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐

Part II SUMMARY OF ACTION

1. ☐ Claims 6-10 are pending in the application.
Of the above claims, are withdrawn from consideration.
2. ☐ Claims have been cancelled.
3. ☐ Claims are allowed.
4. ☐ Claims 6-10 are rejected.
5. ☐ Claims are objected to.
6. ☐ Claims are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on . Under 37 C.F.R. 1.84 these drawings are ☐ acceptable. ☐ not acceptable (see explanation or Notice re Patent Drawing, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on has (have) been ☐ approved by the examiner. ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed on has been ☐ approved. ☐ disapproved (see explanation).
12. ☐ Acknowledgment is made of the claim for priority under 35 USC 119. The certified copy has ☐ been received ☐ not been received
☐ been filed in parent application, serial no. ; filed on .
13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

EXAMINER'S ACTION

08/869,406

DETAILED ACTION

Claim Rejections - 35 USC § 112 Second Paragraph

1. Claims 6-10 rejected under 35 U.S.C. 112, second paragraph, as failing to set forth the subject matter which applicant(s) regard as their invention.

This rejection is hereby withdrawn.

First Paragraph

2. Claims 6-10 rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This rejection is hereby withdrawn.

Claim Rejections - 35 USC § 102

Claims 6-8 remain rejected under 35 U.S.C. 102(b) as being anticipated by Potzschke et al. (U) for the reasons set forth in the previous office actions and the reasons set forth below.

Applicants argue the prior art does not anticipate the claimed invention since the prior art is only an analytical method whereas the claimed method is a preparative method. As evidence, applicants cite the difference in column size and flow rate. Therefore, "since hyperpolymeric hemoglobins have not been investigated with regard to their size and molecular weight distribution up to the present invention, it could not have been foreseen that a method directed to an analytical scale can easily be transformed to a preparative scale." Finally, applicants also state that Potzschke only cites fractionation with regard to ultrafiltration, which however, is completely different from chromatography and not the subject matter of the present claims.

Applicant's arguments filed 03-30-98 have been fully considered but they are not persuasive.

Applicants have stated that the claimed invention is a preparative method and thus the prior art does not anticipate them. However, the claims do not limit the scope as a preparative method, rather the claims rejected correspond to either a preparative method or an analytical method. Applicants also made a reference to the lack of

chromatography teaching. It is unclear if the applicants intended to mean that the reference does not teach a chromatographic step and thus do not anticipated the claimed method. If applicants did intend to mean as such, then applicants are incorrect since the reference clearly states that the crosslinked hemoglobin is purified with Sephacryl S-400 high resolution gel with a NaCl, HEPES buffer, and NaN₃ as the eluent electrolyte solution.

The rejection is maintained.

Claim Rejections - 35 USC § 103

Claims 6-10 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Potzschke et al.(U) in view of Bonhard et al. for the reasons set forth in the previous office actions and the reasons set forth below.

It is believed that for the primary reference of Potzschke et al. applicants have applied the same arguments as stated for the rejection above. For the Bonhoard reference, applicants argue that the reference does not teach the conditions, i.e. time of fractionation and concentration, as currently claimed in the instant application. Secondly, the object of Bonhard are completely different from applicants. Bonhard et al. teach the separation of un-cross-linked hemoglobin solution from cross-linked hemoglobin product. Bonhard et al. is not concerned with a "method to separate molecularly uniform hemoglobin hyperpolymers from known hemoglobin hyperpolymers solution having a broad distribution of different molecular weights."

Applicant's arguments filed 03-30-98 have been fully considered but they are not persuasive.

As stated above, the reference of Potzchke et al. still read on the claims since the claims do not distinguish between preparative method and analytical method. For the secondary reference, applicant is reminded that to establish a prima facie case of obviousness, motivation to combine a reference need not be identical to applicants. In this case the motivation to use ammonium sulfate is to separate uncross-linked hemoglobin from cross-linked hemoglobin. It is established in the art that uncross-linked hemoglobin readily dissociates in the two α - β dimers. The dimers have to low a molecular weight for retention in the circulatory system of the body, and are filtered by the kidneys for excretion with urine. The unmodified hemoglobin have also been induces significant nephrotoxicity. Therefore, one of ordinary skill ~~would be motivated to use ammonium sulfate to remove any uncross-linked hemoglobin so as to avoid nephrotoxicity.~~

As for the difference cited by the applicant in length of time size of columns, and flow rate, it should be noted that the

only limiting factor in the claims is the length of time to use ammonium sulfate. The claims do not make any reference to column size or flow rate. However, even if the claims recited such limitation, it would have been obvious to optimize such conditions through routine experimentation. As stated in the previous office action, generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. Applicants have not provided ample evidence as to why these parameters could not be optimized and have not established a criticality.

Rejection Maintained.

3. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).


A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

4. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anish Gupta whose telephone number is (703) 308-4001.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang, can normally be reached on (703) 308-0254. The fax phone number of this group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Anish Gupta


CECILIA J. TSANG
SUPERVISORY PATENT EXAMINER
GROUP 1850